REMARKS

In the Office Action, the election in response to restriction was noted and commented on, the Information Disclosure Statement previously submitted was not considered due to alleged lack of reference copies, the specification was objected for alleged lack of SEQ ID NOs for the presented sequences, and claims 1, 2, 6, 9, 12-15, 17, 22, 27, 28 and 30-32 were rejected under 35 USC 112, first paragraph as allegedly lacking enablement.

Change of Address

Applicants request entry of the Power of Attorney and Change of Address form submitted herewith.

Restriction/Election

In the response to restriction, Applicants indicated that claims 22-24 were generic to the elected invention. As noted in the Office Action, claim 23 reads "the sample comprises double-stranded polynucleotides" (emphasis added). That the sample comprises double-stranded polynucleotides does not exclude that the sample can also contain single-stranded polynucleotides, as "comprises" is open claim language. Claim 23 can therefore read on instances where single-stranded polynucleotide is present in the sample.

Regarding claim 24, amplification does not require that exclusively double-stranded polynucleotides be produced. As the application sets forth at pages 16-19, in particular in the paragraph bridging pages 17-18, a number of amplification methods and strategies are known in the art. Many of these strategies produce an excess of one polynucleotide strand. For example, even PCR when performed with an excess of one amplification primer will produce excess copies of one strand, which copies are necessarily single-stranded. Claim 24 can therefore read on instances in which the target polynucleotide is produced via amplification.

Claims 23 and 24 are therefore generic to the elected invention. Reconsideration of their withdrawal is respectfully requested.

Information Disclosure Statement

The Office Action alleged that no copies of the cited references were provided. Applicants' representative exchanged voicemails with the Examiner informing him that the references were filed and that a copy of the postcard from that filing indicating the references

were received by the PTO is in his possession. The Examiner indicated via voicemail that the references have been located at the PTO.

Consideration of the Information Disclosure Statement is respectfully requested.

Objection to the Specification

The Office Action alleged that amino acid and/or nucleic acid sequences were presented without the requisite SEQ ID NOs, citing pages 24 and 32. This objection is traversed.

The Examiner is referred to the preliminary amendment received by the PTO on Nov. 18, 2005, which is identified on the "Transaction History" and "Image File Wrapper" tabs on the PAIR system, along with an indication that the Computer Readable Format is technically good and was entered into the database on Nov. 28, 2005.

In that amendment, Applicants submitted paper and electronic copies of the sequence listing and amended the specification, in particular at pages 24 and 32 as noted in the Office Action.

Entry of the preliminary amendment of Nov. 18, 2005 and withdrawal of this objection is respectfully requested.

The rejections under 35 USC 112, first paragraph

Claims 1, 2, 6, 9, 12-15, 17, 22, 27, 28 and 30-32 were rejected under 35 USC 112, first paragraph as allegedly lacking enablement. This rejection is traversed.

An invention as filed is presumptively enabled. The Training Materials For Examining Patent Applications With Respect To 35 U.S.C. Section 112, First Paragraph-Enablement Chemical/Biotechnical Applications ("Training Materials") teach that:

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
>
> 1. the breadth of the claims,
> 2. the nature of the invention,
> 3. the state of the prior art,
> 4. the level of one of ordinary skill,
> 5. the level of predictability in the art,
> 6. the amount of direction provided by the inventor,
> 7. the existence of working examples, and

8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands,* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement).

   In *Wands*, the court noted that there was no disagreement as to the facts, but merely a disagreement as to the interpretation of the data and the conclusion to be made from the facts. *In re Wands,* 858 F.2d at 736-40, 8 USPQ2d at 1403-07. The court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." Id. at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." Id., 8 USPQ2d at 1407.

   It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of non-enablement must be based on the evidence as a whole. Id. at 737 & 740, 8 USPQ2d at 1404 & 1407.

Training Materials at III.

An enablement rejection requires factual evidence regarding each of the *Wands* factors; generic unsupported assertions do not meet the legal standard for establishing lack of enablement. The *Wands* factors and their characterization in the Office Action are analyzed in turn below.

The breadth of the claims. The pending claims encompass assay methods using a polycationic multichromophore that can interact with a target polynucleotide and can transfer energy to a signaling chromophore conjugated to a sensor polynucleotide-binding protein when brought into proximity thereto by binding of the sensor to the target polynucleotide, if present.

Regarding this factor, the Office Action simply stated that the "claims fairly encompass the detection of any and all manner of nucleic acids." This has no bearing on the enablement of the claims. The Office Action further stated that nothing would preclude binding to non-target molecules, and alleged that the application does not teach a skilled artisan would not be able to differentiate between binding to non-target and target nucleic acids. This is false. The application contains control experiments exemplifying binding to specific target sequences and to specific sensor PBPs (see the Examples). One of skill in the art is capable of performing control experiments. Furthermore, as is known in the biological arts, the selective binding nature

of many polynucleotide specific binding proteins yields exquisite selectivity in everything from cell replication, gene expression, and viral replication.

Additionally, new claim 33 recites that the sensor PBP "preferentially binds" to the target polynucleotide. This is supported at page 11 of the application as filed, in the discussion of the target polynucleotide, the sensor PBP, and in the examples. No new matter is added. This claim is believed to overcome any possible objection based on non-specific binding.

The nature of the invention. As set forth above, the nature of the invention is a biotechnological assay method using a polycationic multichromophore that can interact with a target polynucleotide and can transfer energy to a signaling chromophore conjugated to a sensor polynucleotide-binding protein when brought into proximity thereto by binding of the sensor to the target polynucleotide, when present.

The Office Action alleged, without support, that the method employs non-specific binding of nucleic acids. The examples demonstrate the ability of the invention to provide a method of detecting a target polynucleotide in a sample using a sensor polynucleotide-binding protein. Nothing further is required by the claims.

Furthermore, if Applicants wish to use a sensor PBP that can bind to multiple target polynucleotides, that is within the scope of the invention. A sensor for generic polynucleotides in a sample has utility in a number of bioassays, for example for contamination of biological products. The statements in the Office Action relate to scope and utility, not to the nature of the invention.

The state of the prior art. The state of the prior art was such that a number of specific interactions were known in the art between polynucleotides and proteins that bind to them. No analysis of this factor, which argues for enablement, was provided in the Office Action. Therefore the Wands analysis in the Office Action cannot support an enablement rejection, as all Wands factors were not analyzed.

The level of one of ordinary skill in the art. The level of one of skill in the art of biotechnology is high, requiring at least a Ph.D in molecular biology, biochemistry or a related discipline, or equivalent experience. This factor, which also argues towards enablement, was not analyzed in the Office Action. The rejection is unsupported on this grounds, as well.

The level of predictability in the art. The level of predictability in the art is such that a number of specific polynucleotide/binding protein interactions are known in the art, and suitable binding conditions are discernable by one of skill for a given target polynucleotide and a corresponding binding protein. Following the examples and teachings in the application, it is predictable that one of skill could perform the invention with other target polynucleotides and polynucleotide binding proteins.

The Office Action's statement that "[t]he area to which the invention belongs ... is inherently unpredictable and requires greater level of enablement" does not contain any factual relation to the invention at hand, and additionally cites case law that is dated in relation to the date of invention, occurring more than 30 years prior. The predictability of the specific technology at issue in Fisher more than 30 years earlier has no bearing on the predictability of the invention claimed here. As no factual analysis of this Wands factor was provided, the rejection is also unsupported on this ground.

The amount of direction provided by the inventor. The application presents working examples of the invention and considerable teachings regarding other systems comprising polynucleotide binding proteins and corresponding polynucleotides to which the methods of the invention can be adapted (see pages 22-24), including specific examples of sequences which can be used. No discussion of this direction in the application was provided in the Office Action.

The Office Action states only that "[t]he amount of guidance is extremely limited, leaving the fundamental issues of full enablement to the pubic [sic] to resolve." This is not factual evidence relating to the guidance presented for this invention in this application, and does not meet the standard required for a Wands analysis of each factor.

The existence of working examples. Working examples of the methods are provided, using both control nucleic acid sequences and control polynucleotide binding proteins to demonstrate selective binding and signaling. The Office Action stated that no working examples were provided where any target RNA can be detected are provided; however, this is incorrect. The examples demonstrate selective binding to Tar RNA of the Tat-C labeled probe (e.g., see Example 4). It is not a requirement that Applicants provide all possible working examples to demonstrate enablement.

The Quantity Of Experimentation. The Office Action simply stated that "[t]he quantity of experimentation is vast, on the order of several man-years, with little if any reasonable expectation of success." This statement does not contain any factual evidence relating in any way to any part of the invention. Enablement requires that one of skill be required to perform only one embodiment of the invention without undue experimentation. One of skill could perform one embodiment of the invention following the teachings in the application without undue experimentation. No evidence of record indicates otherwise.

It has never been a requirement that one must make all possible species falling within a generic claim. Broad claims have long been permitted in the pharmaceutical and polymer chemistry fields where huge numbers of individual embodiments fall within the claim scope. As long as the range of species can be prepared using known techniques, such claims are enabled, and provide an appropriate scope of protection to incentivize invention. The law has similarly been applied in the biotechnological arts, where an applicant was required only to enable the production of one antibody having the claimed functional characteristics: "Wands carried out this entire procedure three times, and was successful each time in making at least one antibody that satisfied all of the claim limitations." In re Wands, 8 USPQ 2d 1400, 1407 (Fed. Cir. 1988), emphasis added.

MPEP Section 2164.08 states (emphasis added):

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
>
> As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971).
>
> The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of the enablement involves two stages of inquiry. The first is to determine how broad the claim is with respect to the disclosure. The entire

> claim must be considered. The second inquiry is to determine if one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation.
>
> How a teaching is set forth, by specific example or broad terminology, is not important. In re Marzocchi, 439 F.2d 220, 223-24 169 USPQ 367 , 370 (CCPA 1971). ... In In re Goffe, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976), the court stated:
>
> [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.

Applicants are the first to disclose the use of a labeled sensor polynucleotide-binding protein to detect a target polynucleotide utilizing energy transfer with a polycationic multichromophore. Applicants are entitled to claims which bear a reasonable relationship to the invention they have disclosed to adequately protect their invention. Restricting them to their preferred materials would not serve the constitutional purpose of promoting progress in the useful arts. This rejection is contrary to MPEP 2164.08 and unconstitutional.

Generic claims to antibodies were found enabled in *In re Wands*, even though the individual number of antibodies which can be produced through variability in genetic and immunological recombination includes vast numbers of possible structures, because one of skill following the teachings of Wands could produce one antibody meeting the claim limitations without undue experimentation. *Wands* at 1407.

For the foregoing reasons, the claimed invention is enabled. The rejection under 35 USC 112, first paragraph is unsupported, and withdrawal of the rejection is respectfully requested. A telephonic interview is requested prior to any subsequent action other than allowance.

Respectfully submitted,
/David W. Maher/
David W. Maher, Ph.D.
Reg. No. 40,077
858-228-7829